DOCKET NO.: ISIS-5024 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Muthiah Manoharan, Phillip Dan Cook and Clarence Frank Bennett

Serial No.: Not Yet Assigned Group Art Unit: Not Yet Assigned

Filed: Herewith Examiner: Not Yet Assigned

For: DERIVATIZED OLIGONUCLEOTIDES HAVING IMPROVED UPTAKE AND

OTHER PROPERTIES

Assistant Commissioner for Patents Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT

Prior to examination of the above-identified application, Applicants respectfully request that the following amendments be entered.

In the Claims:

Please ADD the following new Claims 45 through 53.

- --45. A method of effecting cellular uptake of a compound having a plurality of linked nucleosides, comprising contacting an organism with said compound wherein said compound includes at least one heterocyclic base functionalized nucleoside having a steroid molecule, an enzyme, a peptide, a protein, or a vitamin, linked to the heterocyclic base of the nucleoside.
- 46. The method of claim 45 wherein said heterocyclic base functionalized nucleoside is functionalized with a steroid molecule.

- 47. The method of claim 45 wherein said heterocyclic base functionalized nucleoside is functionalized with an enzyme, a peptide or a protein.
- 48. The method of claim 45 wherein said heterocyclic base funtionalized nucleoside is functionalized with a vitamin.
- 49. A method of effecting cellular uptake of a compound having a plurality of linked nucleosides, comprising contacting an organism with said compound wherein said compound includes at least one inter-strand nucleoside having a steroid molecule, an enzyme, a peptide, a protein, or a vitamin linked to an inter-strand linkage linking said inter-strand nucleoside to an adjacent nucleoside.
- 50. The method of claim 49 wherein said inter-strand nucleoside has a steroid molecule linked to an inter-strand linkage linking said inter-strand nucleoside to an adjacent nucleoside.
- 51. The method claim 50 wherein said inter-strand linkage is not the inter-strand linkage between the first and the second nucleosides at the 3' terminus or the 5' terminus of said oligonucleotide.
- 52. The method of claim 49 wherein said inter-strand nucleoside has an enzyme, a peptide or a protein linked to an inter-strand linkage linking said inter-strand nucleoside to an adjacent nucleoside.

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53. The method claim 49 wherein said inter-strand nucleoside has a vitamin linked to an inter-strand linkage linking said inter-strand nucleoside to an adjacent nucleoside.--

REMARKS

Claims 45 through 53 have been added.

Date: FEB. 11, 2002

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